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REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated March 16, 2001.

The Examiner has objected to the Abstract as an abstract of the invention. Applicants have above amended the Abstract so that it is an abstract of the disclosure in accordance with MPEP § 608.01(b).

The Examiner has objected to the Specification because it lacks sequence identifiers, specifically at cited pages 14, 44 and 54. Applicants have above amended the Specification to add the proper and appropriate SEQ ID NO:s.

Replacement paragraphs for all of the indicated changes are set forth above, and entry and favorable consideration thereof is requested.

Status of the Claims

Claims 50-59 are pending in the application. Claim 50, which is withdrawn from consideration, has been cancelled. Claims 51-59 have been amended. Support for the amended claims can be found generally through Applicants' specification.

The §101 Rejection

The Examiner has rejected Claims 51, 52 and 58 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter because the claims do not require that the antibodies have been isolated. Applicants have above amended claims 51, 52 and 58 to refer to "isolated" antibody. Applicants submit that the Examiner's § 101 rejection is now obviated and should be withdrawn.

The §102 Rejection

The Examiner has rejected Claims 51 and 52 under 35 U.S.C. § 102(b) as unpatentable over Redpath et al. [J. Biol. Chem. 1996, Vol. 271(29),pp. 17547-17554], remarking that Redpath et al. teaches anti-peptide antibodies that were raised against peptides of rabbit eEF-2

kinase reacted with rat eEF-2 kinase, which is 90% identical to instant SEQ ID NO:2. The Examiner asserts that since these antibodies raised against rabbit sequenece reacted with the rat protein, they would also react with the "nearly identical sequence" in the human and mouse proteins, and would also anticipate the limitations of Claims 51 and 52. Applicants respectfully disagree and submit that antibodies raised against the rabbit eEF-2 kinase do not anticipate per se antibodies against human or mouse eEF-2 kinase protein. Nonetheless, in an effort to facilitate prosecution and without prejudice, Applicants have above amended Claims 51 and 52 to more particularly refer to specific eEF-2 antibodies, which are not anticipated by Redpath et al. The antibodies as now recited to specifically bind to the noted eEF-2 kinase are clearly distinct from the antibodies of Redpath et al. Redpath does not disclose or suggest the particular eEF-2 kinase sequences of the instant Application and further does not disclose or suggest the specific antibodies thereto.

The §103 Rejections

The Examiner has rejected Claim 51 and 53-59 under 35 U.S.C. § 103(a) as unpatentable over Redpath et al. [J. Biol. Chem. 1996, Vol. 271(29), pp. 17547-17554], in view of Harlow and Lane, Antibodies, 1988.

With regard to Claims 51 and 53-59, drawn to monoclonal antibodies and a cell line that produces such antibodies, the Examiner comments that, while Redpath teaches anti-peptide polyclonal antibodies but fails to teach monoclonal antibodies or immortal cell lines, Harlow and Lane teach generation of monoclonal antibodies and immortal cell lines. The Examiner asserts that it would have been obvious to the skilled artisan to combine these teachings to generate monoclonal antibodies to eEF-2 kinases. Applicants disagree and submit that the combined teachings do not make obvious the claimed antibodies specifcally binding to the references eEF-2 kinase of the invention. Redpath does not disclose or suggest the particular eEF-2 kinase sequences of the instant Application and further does not disclose or suggest the specific antibodies thereto. The knowledge of how to make antibodies in general, as provided by Harlow and Lane, does not make any and all antibodies to any sequence obvious per se, as suggested by the Examiner, particularly wherein the sequence of the protein to which the antibody is

specifically directed is not disclosed or known.

The Examiner further asserts that the combined teachings of Redpath and Harlow and Lane make obvious the labeled antibodies of Claims 55-57. Applicants respectfully disagree and assert that the claimed labeled antibodies of Claims 55-57, in as much as they are distinct from the antibodies of Redpath as noted above, are not made obvious by the combined references.

With regard to Claim 58, drawn to antibody fragments, the Examiner similarly asserts that it would have been obvious to one of ordinary skill to combine the teachings of Redpath et al with those of Harlow and Lane to generate antibody fragments of the Redpath antibodies. Again, Applicants submit that, in as much as the claimed specific anti-eEF-2 kinase antibodies are not anticipated by Redpath et al, the antibody fragments are similarly not made obvious by the combination with Harlow and Lane.

The Examiner rejects Claim 59, drawn to antibodies in pharmaceutical carriers, as obvious in view of the combination of Redpath and Harlow and Lane, stating that it would have been obvious to suspend the antibodies of Redpath in phosphate buffered saline for purposes of iodination and storage. The antibodies of Redpath do not teach or anticipate the instantly claimed specific antibodies and do not make the claimed pharmaceutical compositions obvious in combination with Harlow and Lane.

In addition, the Examiner rejects Claims 51 and 53-59 as they encompass antibodies to the *C. elegans* sequence SEQ ID NO:10 as made obvious by Redpath in view of Harlow and Lane. In this rejection, the Examiner remarks that Redpath teaches a *C. elegans* protein identical to a portion of SEQ ID NO:10 and, while Redpath does not teach such antibodies, it would have been obvious to the skilled artisan, given Harlow and Lane, to generate such antibodies based on the sequence disclosed by Redpath. Applicants respectfully disagree and submit that the combination of Redpath and Harlow and Lane does not make obvious the specific claimed antibodies. The knowledge of how to make antibodies in general does not make any and all antibodies to any known sequence obvious per se, as suggested by the Examiner.

In a further 103 rejection, Claims 51-59 are rejected under 35 U.S.C. 103(a) as unpatentable over Ryazanov et al [PNAS May 1997, vol. 94, pp. 4884-4889] in view of Harlow and Lane. The Examiner remarks that Ryazanov et al teaches human, mouse and *C. elegans*

kinases that are identical to instant SEQ ID NOS: 2, 4 and 10 and, while Ryazanov does not teach antibodies to these sequences, the antibodies are obvious to generate in view of Harlow and Lane's teaching. Applicants respectfully disagree. The knowledge of how to make antibodies in general does not make any and all antibodies to any known sequence obvious per se, as suggested by the Examiner. Applicants further point out that Ryazanov et al which indicates all of the inventors of the present application as authors, and the entire disclosure of which is included in the instant Specification, was published less than one year prior to the date of filing (August 20, 1997) of the instant Application and is therefore also not appropriate as a prior art reference. In as much as Ryazanov et al is not a true prior art reference, it cannot make obvious the antibodies in combination with Harlow and Lane.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's rejections under 35 U.S.C. § 103 are overcome and should be withdrawn.

The Specification Enables the Claimed Invention

The Examiner has rejected Claim 59 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the Specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner asserts that, while Claim 59 is drawn to a pharmaceutical composition comprising an antibody to eEF-2 kinase, the Specification teaches only that preliminary evidence indicates that eEF-2 kinase is upregulated in some cancers (cited p.6, lines 2-4) and teaches on pages 29-31 that antibodies might be used diagnostically. The Examiner further suggests that it would require undue experimentation to use the antibodies as pharmaceutical compositions. Applicants respectfully disagree and submit that the Specification clearly enables the skilled artisan to make and/or use a pharmaceutical composition comprising an eEF-2 antibody.

While some experimentation to make and test such pharmaceutical compositions would be necessary, such experimentation would utilize well known methods and standard skills and would <u>not</u> constitute <u>undue</u> experimentation. With regard to the determination of what is undue experimentation, the PTO and the courts have commented that "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such

experimentation." MPEP § 2164.01, *citing M.I.T. v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). The test of enablement is not whether experimentation is necessary, but whether or not it is undue. *Ibid, citing In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). With regard to this rejection, the Examiner points to the Wands factors, which are to be considered in determining undue experimentation. *Ibid, citing In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). In the present instance: (1) the quantity of experimentation, while significant, is not undue for the skilled artisan; (2) the direction or guidance provided by the specification is sufficient for the skilled artisan and appropriate for the time; (3) working examples are provided; (4) the nature of the invention, including, but not limited to the disclosure of sequences to which antibodies are directed; (5) the extent of prior art available to those skilled in the art with regard to making and testing antibodies was very significant at the time of filing; (6) the relative skill of those in the art is substantial - the courts have determined that, in molecular biology, the level of skill in the art corresponds to that of a Ph.D. with postdoctoral experience; (7) the making, testing and use of the antibodies in pharmaceutical compositions is certainly not unpredictable; and (8) the breadth of the claims is commensurate with the significant skill of those in the art. The Examiner particularly and correctly points out that Applicants have taught evidence of upregulation of eEF-2 kinase in cancers and diagnostic use of the antibodies. In view of the foregoing, Applicants submit that given the guidance provided by the specification, the well known criteria or parameters for making and testing of antibodies, and the significant level of skill in the art a person of ordinary skill in the art could, without undue experimentation, make and use the pharmaceutical compositions encompassed by the claims.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C.§ 112, first paragraph is overcome and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,
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Complete Listing of Claims in Application U.S.S.N. 09/994,485

Claims 1-49 (canceled)

Claim 50 (canceled)

51. (currently amended) An isolated antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10.

52. (currently amended) An isolated antibody which specifically binds to a human eEF-2 kinase capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising the amino acid sequence of SEQ ID NO:2.

53. (currently amended) A monoclonal antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10.

54. (currently amended) An immortal cell line that produces a monoclonal antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10.

55. (currently amended) An isolated antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, said antibody labeled with a detectable label.

56. (currently amended) The antibody of Claim ~~54~~ 55 wherein the label is selected from enzymes, chemicals which fluoresce and radioactive elements.

57. (currently amended) A radioactively labeled antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10.

58. (currently amended) An active fragment of an isolated antibody which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, said active fragment selected from the group of Fab, Fab', $F(ab')_2$ and Fv fragments.

59. (currently amended) A pharmaceutical composition comprising:

A. a therapeutically effective amount of an antibody ~~directed~~ which specifically binds to a eukaryotic elongation factor-2 kinase (eEF-2 kinase) capable of phosphorylating an amino acid within an alpha helical domain of eukaryotic elongation factor-2 (eEF-2), said kinase comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:10, or an active fragment of said antibody; and,

B. a pharmaceutically acceptable carrier.